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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
CARTER, KENDRA D	
ART UNIT	PAPER NUMBER
1627	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/582,499	BRUECK-SCHEFFLER, ANTJE	
	Examiner	Art Unit	
	KENDRA D. CARTER	1627	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 January 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10 and 12-41* is/are pending in the application.

4a) Of the above claim(s) *21-41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 12-20* is/are rejected.

7)☒ Claim(s) *2* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date _____
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Examiner acknowledges the applicant's remarks and arguments of January 19, 2011 made to the office action filed July 20, 2010. Claims 1-10 and 12-41 are pending. Claims 1 and 2 are amended, and claims 21-41 are withdrawn. Claim 10 is cancelled.

For the reasons in the previous office action and below, the Applicant's arguments of all previous 35 U.S.C. 103(a) rejections were found not persuasive, thus the rejections are upheld.

Due to the amendments, the modified 35 U.S.C. 103(a) rejections are below. The Applicant's arguments are also addressed below.

Claim Objections

Claim 2 is objected to because of the following informalities: the claim should be amended such that in line 4, after "optionally further", "one or more" should be added. Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1) Claims 1-4, 7-9 and 11-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nishibe et al. (US 2006/0166953 A1) in view of Saidi et al. (US 6,241,969 B1) and Lintz et al. (US 2004/0247628 A1).

Nishibe et al. teach a ciclesonide containing sterile aqueous suspension sterilized by autoclaving (see abstract; addresses claims 1, 3 and 4). The suspension may comprise suspending agents and wetting agents such as hydroxypropylmethylcellulose (i.e. non-ionic excipients and suspending agent; see paragraphs 38 and 42; addresses claims 1, 9, 11 and 13). Ciclesonide is dispersed in an aqueous medium including the excipients (see page 3, paragraph 42, lines 5-8) to give a white uniform aqueous suspension before being autoclaved at 115 degrees C for 30 minutes, at 121 degrees C for 20 minutes or at 126 degrees C for 15 minutes (see page 3, paragraph 43 and 49; addresses claims 15-19).

Nishibe et al. does not specifically teach that the composition is suitable for nebulization (claim 1), nor that the composition comprises the specific non-ionic agent in claims 7 and 8. Nishibe et al. also does not teach specifically teach at least one non-ionic agent for adjusting osmolality (claims 1 and 2), nor the osmolality range in claim 20. Nishibe et al. does not specifically teach the motivation for the specific suspending agent polysorbate (claim 14), nor the pH modifying agents of claim 12.

Saidi et al. teach an aqueous composition to treat ailments and diseased of the respiratory tract, particularly the lungs, comprising a cortiscosteroid that can be delivered through a nebulizer (see abstract). The composition comprises an osmolality agent such as glucose such that the osmolality of the composition is from about 280-300 mosmol/kg (see column 7, lines 3-9; addresses claims 1, 7, 8 and 20). The composition also comprises a surfactant such as sorbitan esters (Tween series; i.e. polysorbate; see column 8, line 57; addresses claim 14).

Lintz et al. teach pharmaceutical kits for the preparation of liquid composition that are administered as aerosols through nebulization (see abstract and paragraph 18). Drugs to be delivered include ciclesonide (see paragraph 19) that can be administered with excipients such as citric and tartaric acid to adjust the pH (see paragraph 25) and surfactants to increase the wettability of the active compound or to improve the dissemination of the aerosol droplets in the lungs (see paragraph 27). Preferable surfactants include Tween 60 (i.e. polysorbate; see paragraph 27, last two lines).

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the method of Nishibe et al. and providing the composition in a nebulizer because Saidi et al. teach that compositions can be made with cortiscosteroids to be delivered through a nebulizer to provide treatment for ailments and diseases of the respiratory tract (see abstract).

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the method of Nishibe et al. and providing the osmolality agents of claims 1, 2, 7 and 8 and at the osmolality range of claim 20 because Saidi et al. teach nebulizer compositions comprising cortiscosteroids that have an osmolality agent such as glucose such that the osmolality of the composition is from about 280-300 mosmol/kg (see column 7, lines 3-9). Buffers may be used to adjust the pH (see column 6, lines 64-66).

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the method of Nishibe et al. in view of Saidi et al. and providing an organic acid of claim 12 as a pH modifying agent because Saidi et al. and Lintz et al. teach that nebulized composition of drugs such as ciclesonide can be administered with pH modifiers. Particularly, Lintz et al. teach that organic acids such as citric and tartaric acid to adjust the pH (see abstract and paragraphs 18, 19 and 25).

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the method of Nishibe et al. and providing the specific suspending agent polysorbate because Lintz et al. teach that nebulized composition of drugs such as ciclesonide can be administered with excipients such as surfactants to increase the wettability of the active compound or to improve the dissemination of the aerosol droplets in the lungs (see paragraph 27). Preferable surfactants include Tween 60 (i.e. polysorbate; see paragraph 27, last two lines).

In regards to claim 16, since Nisibe et al. adds ciclesonide to the non-ionic agent, it would be obvious to one skilled in the art to also add ciclesonide to the non-ionic agent Saidi et al. to adjust the osmolality.

2) Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nishibe et al. (US 2006/0166953 A1) in view of Saidi et al. (US 6,241,969 B1) and Lintz et al. (US 2004/0247628 A1) as applied to claims 1-4, 7-9 and 11-20, in further view of Allen et al. (J Allergy Clin Immunol, Sept 2003, vol. 112, no. 3, pp. s7-s40) and ACS Registry (Feb 1995, pg 1).

The teachings of Nishibe et al., Saidi et al. and Lintz et al. are as taught above for claims 1-4, 7-9 and 11-20.

Nischibe et al., Saidi et al. and Lintz et al. do not teach the ciclesonide derivatives of claim 5.

Allen et al. teach that CIC-AP is the active metabolite of ciclesonide in the lungs (see figure 10).

ACS Registry identifies CIC-AP as 16α,17-(22R,S)-cyclohexylmethylene-dioxy-11β,21-dihydroxypregna-1,4-diene-3,20-dione, and as the active metabolite of ciclesonide.

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the method of Nishibe et al. in view of Saidi et al. and providing the ciclesonide derivatives of claim 5 because Allen et al. and the ACS registry identify 16α,17-(22R,S)-cyclohexylmethylene-dioxy-11β,21-dihydroxypregna-1,4-diene-3,20-dione as the active metabolite of ciclesonide (see page 1, paragraph 6).

3) Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nishibe et al. (US 2006/0166953 A1) in view of Saidi et al. (US 6,241,969 B1) and Lintz et al. (US 2004/0247628 A1) as applied to claims 1-4, 7-9 and 11-20, in further view of Sambuco et al. (US 2005/0175546 A1).

The teachings of Nishibe et al., Saidi et al. and Lintz et al. are as taught above for claims 1-4, 7-9 and 11-20.

Nischibe et al., Saidi et al. and Lintz et al. do not teach the particle size of ciclesonide as in claim 6.

Sambuco et al. teach an aqueous suspension of sterile micronized drug particles, particularly corticosteroids such as ciclesonide, administered by inhalation, which produces homogenous dispersions of particles characterized by optimal size and size distribution (see abstract and paragraph 29). The particles are preferably less than 7μm (see paragraph 33), which can more easily dissolve in the lung fluids and penetrate into the cells in a better way, giving rise to a prolonged activity (see paragraph 39).

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the method of Nishibe et al. in view of Saidi et al. and providing the particle sizes of claim 6 because Sambuco et al. teach that particle sizes less than 7μm (see paragraph 33) can more easily dissolve in the lung fluids and penetrate into the cells in a better way, giving rise to a prolonged activity (see paragraph 39).

Response to Arguments

Applicant's arguments have been fully considered but they are not persuasive.

> The Applicant's argue that there is no motivation to combine the Nishibe et al., Saidi et al. and Lintz et al. references to choose only "non-ionic excipients" Particularly, the suspension that is taught by Nishibe et al. is not intended for inhalation or nebulization (see paragraph 46). Further, the Nishibe et al. reference is faced with the technical problem of providing a sterile aqueous ciclesonide suspension that does not suffer from clogging and a suspension that is suitable for nebulization, i.e. inhalative administration.

The Examiner disagrees because the motivation to combine the references is to make a sterile inhalation formulation of ciclesonide. First, Nishibe et al. provides the teaching of a method to sterilize a suspension of ciclesonide. Although the compositions of Nishibe et al. are not administered via inhalation or nebulization, Saidi et al. provides the motivation to make a nebulizer formulation of ciclesonide. Particularly, Saidi et al. teach that composition can be made with cortiscosteroids to be deliver through a nebulizer to provide treatment for aliments and diseases of the respiratory tract (see abstract). Lintz et al. provides the teaching that nebulized compositions of drugs such as ciclesonide can be administered with excipients such as surfactants to increase the wettability of the active compound or to improve the dissemination of the aerosol droplets in the lungs (see paragraph 27). In regards to the technical problem, Nishibe et al. overcomes the problem by providing a uniform sterilized suspension (see paragraph 2). Further, Sambuco et al. is used to teach the

importance of particle size when administering to the lungs, which is used to reject claim 6. The use of only non-ionic excipients will be addressed below

> The Saidi et al. and Lintz et al. references does not teach autoclaving, so the reference cannot provide any motivation to solve the technical problems associated with autoclaving. The Applicant further argues that there is no teaching in the Nishibe et al., Saidi et al., Lintz et al. and Sambuco references to select only non-ionic agents. Saidi et al. show very little difference between those solutions containing sodium chloride and those without sodium chloride (see example 5). On the other hand the Applicants have demonstrated that suspensions containing ionic agents rendered large white agglomerates that would not be suitable for nebulization (see example 7 in specification). Further, Sambuco et al. does not address any of the technical problems associated with autoclaving, nor cure the deficiencies of Nishibe et al., Saidi et al. and Lintz et al.

The Examiner respectfully disagrees, and notes that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). First, Saidi et al. is used to teach that non-ionic and ionic osmotic agents are known to be used in the art to adjust the osmolality of a composition from about 280-300 mosmol/kg for cortiscosteroid formulations (see column 7, lines 3-9). Second, example 5 does not use ciclesonide nor compare it with glucose. Third, one skilled in the art would have the ability and skill to test for the best osmotic agent to render the best result for nebulization based on the teachings of Nishibe et al., Saidi et al., Lintz et al. and Sambuco et al. Selection of a known material based on its suitability for its intended use is obvious. Particularly, knowing the technical problem associated with autoclaving,

Nishibe et al. provides a uniform suspension of ciclesonide and Saidi et al. provides the motivation and materials of providing a formulation such as Nishibe et al. in a nebulized form.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KENDRA D. CARTER whose telephone number is (571)272-9034. The examiner can normally be reached on 9:00 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Kendra D Carter
Examiner, Art Unit 1627

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